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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/577,074	05/07/2007	James M. Cregg	57015US (67858.701501)	9018

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HUNTON & WILLIAMS LLP
INTELLECTUAL PROPERTY DEPARTMENT
1900 K STREET, N.W.
SUITE 1200
WASHINGTON, DC 20006-1109

EXAMINER

VOGEL, NANCY TREPTOW

ART UNIT	PAPER NUMBER
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1636

MAIL DATE	DELIVERY MODE
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03/18/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/577,074	Applicant(s) CREGG ET AL.	
	Examiner NANCY VOGEL	Art Unit 1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-21 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-21 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. ____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>3/27/07, 4/16/08</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claims 1-21 are pending in the case.

Receipt of the Information Disclosure Statements on 4/16/08 and 3/27/07 is acknowledged.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 4-9, 11-13, are rejected under 35 U.S.C. 102(b) as being anticipated by Robinson et al. (US Patent 6,204, 023).

Robinson et al. disclose a method of producing a secreted heteromultimeric protein which is an antibody, in which a first cell which is haploid is transformed with a first plasmid encoding a light chain gene, and a second haploid cell is transformed with a second plasmid encoding a heavy chain gene, and the cells are mated to form a diploid cell, which secretes the heteromultimeric antibody protein (See col. 15 line 38-16, line 55). The reference discloses evaluating for level of production (col. 15 lines 50-55). The reference discloses expression of libraries (see col. 29-30).

Claim Rejections - 35 USC § 103

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The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-9, 11-13, 15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robinson et al. (US Patent 6,204,023) as applied to claim 1, 4-9, 11-13 above, and further in view of Choudary et al. (WO 00/23579).

Robinson et al. is cited for the reasons set forth above. The difference between the reference and the instant claims is that a specific yeast strain, i.e. Pichia, is disclosed; and inducible promoters are used. However, Choudary et al. disclose the expression of antibodies in Pichia strains (See abstract; see pages 3-4,). Inducible promoters are used (page 6). The same promoter for each subunit is used (page 6). It would have been obvious to one of ordinary skill in the art to have used Pichia strains as disclosed by Choudary et al. in the method disclosed by Robinson, since Robinson

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generally discloses that any yeast strain may be used, and since Choudary disclose the advantages for using Pichia for the production of antibodies. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 1-9, 11-14, 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Robinson et al. as applied to claims 1, 4-9, 11-13 above, and further in view of Zamost (US Patent 6,258,559).

Robinson et al. is cited for the reasons set forth above. The difference between the reference and the instant claims is that a specific promoter, which is constitutive GAP promoter, is recited, and that minimal media is used for culturing. However, the GAP promoter is known in the art as is taught in Zamost (see col. 18-19). Growth of Pichia strains for production of recombinant proteins in minimal media is also taught by Zamost (see col. 1-2). It would have been obvious to one of ordinary skill in the art to have modified the method of Robinson et al. to utilize a known constitutive promoter such as GAP as disclosed by Zamost, since both references concern the production of recombinant proteins in yeast, and since the use of any particular promoter for the properties known to be associated with that promoter, was well known in the art. It would have been further obvious to culture Pichia using minimal media as disclosed by Zamost, in order to obtain the benefits disclosed by Zamost which include better growth and yield. Based upon the teachings of the cited references, the high skill of one of

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ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

.

Claim 21 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention..

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is undue include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The nature of the invention is a method of producing secreted antibodies using yeast cells as hosts, in which a particular concentration of antibodies (100 mg/liter) is produced.

The state of the prior art: The prior art discloses that it is unpredictable whether any particular level of recombinant protein will be produced, depending on many unpredictable factors. For example, Choudary et al. (WO 00/23579) discloses that levels of antibodies produced in *Pichia* are 10-36 mg/liter; and that in other systems antibody fragments may be produced at 200 mg/l, but that complete antibodies are produced at lower levels and that in fact, the levels exemplified are the higher than any previously reported (page 25). Therefore, it is not routine to produce 100 mg/l of complete antibodies in recombinant yeast.

Existence of working examples: the specification discloses an example of producing antibodies using the claimed method, but does not disclose the yield. Furthermore, applicants state that high levels of antibodies will be produced, but does not give an example of such yields.

The amount of direction or guidance by the invention: The amount of guidance provided is limited to the construction of the yeast cells and there is no further guidance to obtain the high level of production claimed.

Quantity of experimentation required would be high, since unpredictability would be involved in methods and conditions of cell culture, expression system used, strain variation, and particular size and nature of recombinant protein expressed, would all need to be manipulated to attempt to obtain the high level of product claimed, with little predictability for success.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

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The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 10 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 10 is vague and indefinite in its recitation of "spheroplast fusion of said first and second haploid", since the claim is dependent on claim 9, which recites that the diploid cell is formed by mating said haploid cells.

Claim 16 is vague and indefinite in the recitation of "said promoter is a GAP promoter", since in the claim on which this claim depends, two promoters are recited and therefore it is not clear which promoter is intended.

Claim 17 is vague and indefinite in the recitation of "optimized signal sequence" since this is a relative term since it is not clear what the optimization is compared to.

Claim 20 is vague and indefinite in the recitation of "low temperature", since it is not clear what is intended by this relative term. Therefore the intended metes and bounds are not clear.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NANCY VOGEL whose telephone number is (571)272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone

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number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/
Primary Examiner, Art Unit 1636

NV
3/16/09